```
  *      Monday through Friday:      6:30am - 9:00pm            *
  *      Saturday, Sunday, Holidays: 8:30am - 5:00 pm           *
  *                                                             *
  *    The Help Desk staff at this number will handle all APS   *
  *    related questions.                                       *
  * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
  *    >>>>>>>>>>>>> NEW SUNDAY HOURS !!! <<<<<<<<<<<<<         *
  *                                                             *
  *    The APS is available:                                    *
  *            6:30am - 9:00pm Monday through Friday            *
  *            7:30am - 5:00pm Saturday, Sunday, Holidays       *
  *                                                             *
  *      APS is unavailable Thanksgiving Day, Christmas Day,    *
  *      and New Year's Day.                                    *
  *                                                             *
  * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
FILE 'USPAT' ENTERED AT 10:48:33 ON 08 APR 1999

  * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
  *               W E L C O M E   T O   T H E                 *
  *         U. S.   P A T E N T   T E X T   F I L E           *
  * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *

=> s triglyceride?(p)(fibrate or fenofibrate)

         12724 TRIGLYCERIDE?
            31 FIBRATE
            90 FENOFIBRATE
L1          12 TRIGLYCERIDE?(P)(FIBRATE OR FENOFIBRATE)

=> d 1-12


1.  5,880,148, Mar. 9, 1999, Combination of fenofibrate and
vitamin E,
and method of use of same in therapeutic treatments; Alan Dunlap
Edgar,
et al., 514/458, 543 [IMAGE AVAILABLE]

2.  5,859,051, Jan. 12, 1999, Antidiabetic agents; Alan D. Adams,
et al.,
514/469, 307, 415, 457; 546/146; 548/469; 549/283, 462 [IMAGE
AVAILABLE]

3.  5,847,008, Dec. 8, 1998, Method of treating diabetes and
related
disease states; Thomas W. Doebber, et al., 514/708, 706, 866, 909,
910
[IMAGE AVAILABLE]

4.  5,827,536, Oct. 27, 1998, Pharmaceutical dosage formulations of
fenofibrate and their applications; Claude Laruelle, 424/451, 455,
456;
514/962, 975 [IMAGE AVAILABLE]

5.  5,767,066, Jun. 16, 1998, Medical application of bromelain;
Stephen
```

George Barnwell, 514/2 [IMAGE AVAILABLE]

6. 5,545,628, Aug. 13, 1996, Pharmaceutical composition containing fenofibrate; Arthur Deboeck, et al., 514/49; 424/1.73, 456, 463, 478,
490, 492; D24/100 [IMAGE AVAILABLE]

7. 5,246,951, Sep. 21, 1993, New benzoselenazolinone compounds; Vincent
Galet, et al., 514/359, 598, 640; 548/121; 562/899 [IMAGE AVAILABLE]

8. 5,128,331, Jul. 7, 1992, Method for lowering plasma lipid levels or
blood pressure; Lan Nguyen, et al., 514/101, 107, 824 [IMAGE AVAILABLE]

9. 5,043,330, Aug. 27, 1991, Phenol substituted gem-diphosphonate derivatives, process for their preparation and pharmaceutical compositions containing them; Lan Nguyen, et al., 514/107; 558/77, 83,
161; 562/19, 21 [IMAGE AVAILABLE]

10. 4,175,130, Nov. 20, 1979, Oxazole- and thiazole-alkanoic acid compounds; Tsutomu Yamanaka, et al., 514/369, 376; 546/269.7, 271.4;
548/187, 228 [IMAGE AVAILABLE]

11. 4,053,635, Oct. 11, 1977, Substituted amides of 3-methyl-4-phenyl-3-
butenoic acid, with a high hypolipemizing activity; Sergio Gorini, et
al., 514/570; 544/176; 564/182 [IMAGE AVAILABLE]

12. 4,008,324, Feb. 15, 1977, Phenoxyalkylcarboxylic acid salt of 1-cinnamyl-4-diphenylmethyl piperazine, method of preparation and antihypercholesteremic; Gunter Metz, et al., 514/255; 544/396 [IMAGE
AVAILABLE]

=> d 1-12 kwic

US PAT NO: 5,880,148 [IMAGE AVAILABLE] L1: 1 of 12

DETDESC:

DETD(40)

In a first series, the plasma levels of total cholesterol, phospholipids
and **triglycerides** were evaluated. The results obtained, which are collated in Table I below, show that **fenofibrate** administered on its
own causes a significant decrease in the total plasma cholesterol (variation from -31 to -40%), very slightly reduces the plasma phospholipid levels and does not modify the plasma **triglyceride**

levels. When combined with dl-.alpha.-tocopherol acetate, **fenofibrate**
generates the same changes, whereas dl-.alpha.-tocopherol acetate administered on its own is inactive.

DETDESC:

DETD(41)

The results in Table I, which are the mean (n=6).+-.the root-mean-square
error, are therefore consistent with the previously disclosed effects of
fenofibrate and dl-.alpha.-tocopherol acetate on the plasma levels of
total cholesterol, phospholipids and **triglycerides**.

DETDESC:

DETD(47)

. . .

0.65 .+-. 0.10

B) Co-micronized feno-

3 0.49 .+-. 0.02.star-solid.

0.97 .+-. 0.02.star-solid.

0.44 .+-. 0.03

fibrate (37 mg/kg/d)

C) dl-.alpha.-Tocopherol

3 0.74 .+-. 0.03.star-solid.

1.28 .+-. 0.04

0.72 .+-. 0.10

acetate (55 mg/kg/d). . .

0.83 .+-. 0.09

B) Co-micronized feno-

8 0.46 .+-. 0.02.star-solid.

1.09 .+-. 0.02.star-solid.

0.43 .+-. 0.05

fibrate (37 mg/kg/d)

C) dl-.alpha.-Tocopherol

8 0.69 .+-. 0.02

1.18 .+-. 0.05

0.69 .+-. 0.10

acetate (55 mg/kg/d). . .

0.82 .+-. 0.12

B) Co-micronized feno-

15 0.4i .+-. 0.02.star-solid.

1.23 .+-. 0.02

0.69 .+-. 0.05

fibrate (37 mg/kg/d)

C) dl-.alpha.-Tocopherol

15 0.65 .+-. 0.04

1.30 .+-. 0.06

0.86 .+-. 0.08

acetate (55 mg/kg/d). . .

1.16 .+-. 0.05

B) Co-micronized feno-

27 0.43 .+-. 0.02.star-solid.

		1.29 .+-. 0.04
		1.24 .+-. 0.23
fibrate (37 mg/kg/d)		
C) dl-.alpha.-Tocopherol		
	27	0.65 .+-. 0.03
		1.35 .+-. 0.05
		0.94 .+-. 0.11
acetate (55 mg/kg/d). . .		1.30 .+-. 0.07
		0.99 .+-. 0.11

Notes:
(1) Total cholesterol (g/l)
(2) Phospholipids (g/l)
(3) **Triglycerides** (g/l)
(.star-solid.) statistically significant
(p .ltoreq. 0.05)

US PAT NO: 5,859,051 [IMAGE AVAILABLE] L1: 2 of 12

SUMMARY:

BSUM(9)

It . . . acids. PPAR.alpha. is also involved with the activity of fibrates in rodents and humans. Fibric acid derivatives such as clofibrate, **fenofibrate**, bezafibrate, ciprofibrate, beclofibrate and etofibrate, as well as gemfibrozil, produce a substantial reduction in plasma **triglycerides** along with moderate reduction in LDL cholesterol, and they are used particularly for the treatment of hypertriglyceridemia.

US PAT NO: 5,847,008 [IMAGE AVAILABLE] L1: 3 of 12

SUMMARY:

BSUM(9)

It . . . acids. PPARA.alpha. is also involved with the activity of fibrates in rodents and humans. Fibric acid derivatives such as clofibrate, **fenofibrate**, bezafibrate, ciprofibrate, beclofibrate and etofibrate, as well as gemfibrozil, produce a substantial reduction in plasma **triglycerides** along with moderate reduction in LDL cholesterol, and they are used particularly for the treatment of hypertriglyceridemia.

US PAT NO: 5,827,536 [IMAGE AVAILABLE] L1: 4 of 12

SUMMARY:

BSUM(2)

Fenofibrate is a substance which has been used for more than 20 years in most countries of the world for the treatment of endogenous hyperlipidaemias, hypercholesterolaemias and hypertriglyceridaemias in adults. Prolonged treatment with **fenofibrate** at the rate of 300 to 400 mg per day makes it possible to obtain a reduction in total cholesterol of 20 to 25% and a reduction in the levels of **triglycerides** of 40 to 50%. It thus opposes the development of atherosclerosis.

SUMMARY:

BSUM(24)

The usual fatty solvents, such as the mono-, di- and **triglycerides** of C.sub.8 to C.sub.16 fatty acids derived from vegetable oils, have not made it possible to obtain the required **fenofibrate** solubilities. The addition of surfactants, such as polyglycosylated glycerides, substantially improves the solubilities, however.

US PAT NO: 5,767,066 [IMAGE AVAILABLE] L1: 5 of 12

SUMMARY:

BSUM(18)

Isobutyric acid derivatives include bezafibrate, clofibrate, **fenofibrate** and gemfibrozil. These drugs effectively reduce plasma **triglycerides** and VLDL, raise HDL, and can reduce LDL-cholesterol by up to 18%. Isobutyric acid derivatives cause about a 10% incidence. . .

US PAT NO: 5,545,628 [IMAGE AVAILABLE] L1: 6 of 12

SUMMARY:

BSUM(5)

Fenofibrate or P-(4-chlorobenzoyl)-phenoxy isobutyrate isopropyl ester is useful for the treatment of adult patients with very high elevations of serum **triglyceride** levels and/or cholesterol levels. The usual daily dosage is 300 mg which is administered in two or three doses. **Fenofibrate** is absorbed as fenofibric acid which is responsible for the pharmacological activity. Fenofibric acid resulting from the hydrolysis of **fenofibrate** is extensively bound to plasma albumin. The plasma half-life is about 20 hours. Fenofibric acid is excreted predominantly in the. . .

US PAT NO: 5,246,951 [IMAGE AVAILABLE] L1: 7 of 12

SUMMARY:

BSUM(522)

The . . . on the day on which the treatment is started. One group
receives a placebo. The other group of mice receives **fenofibrate** at a
dose of 300 mg.kg.sup.-1 /day. The other groups of mice receive the
products of the invention at a dose of 30 mg.kg.sup.-1 /day. An assay of
triglycerides and total, free and esterified cholesterol reveals a
significant decrease in these parameters, greater than that obtained with
fenofibrate (at a 10-fold higher dose).

US PAT NO: 5,128,331 [IMAGE AVAILABLE] L1: 8 of 12

DETDESC:

DETD(156)

With . . . close to man (generally greater than 150 mg/dl). For example, in mice receiving a normal diet the plasma cholesterol and **triglyceride** levels are in the range of 100 mg/dl, whereas for rat the comparative values are close to 50 mg/dl. Other. . . a relevant
model for testing new agents in comparison to drugs known to be efficacious in human hyperlipidemia (Effects of **Fenofibrate**, Gemfibrozil and Nicotinic Acid and Plasma Lipoprotein Levels in Normal
and Hyperlipidemic Mice, a Proposed Model for Drug Screening. Olivier,.
. .

DETDESC:

DETD(176)

TABLE 3

HYPOLIPIDEMIC ACTIVITY OF DIPHOSPHONATES OF FORMULA (I) AND REFERENCE DRUGS

Compounds (I)	Cholesterol (% control)	**Triglycerides** (% control)
1	-2	-28
2	+6	-17
4	-12. . .	
43	-5	-14
46	+1	-12
47	-31	-45

48	-21	-36
Reference Drugs		
Clofibrate	+4	-5
Gemfibrozil	-7	-35
Fenofibrate	-15	-2

US PAT NO: 5,043,330 [IMAGE AVAILABLE] L1: 9 of 12

DETDESC:

DETD(394)

With . . . close to man (generally greater than 150 mg/dl). For example, in mice receiving a normal diet the plasma cholesterol and **triglyceride** levels are in the range of 100 mg/dl, whereas for rat the comparative values are close to 50 mg/dl. Other. . . a relevant
model for testing new agents in comparison to drugs known to be efficacious in human hyperlipidemia (Effects of **Fenofibrate,** Gemfibrozil and Nicotinic Acid on Plasma Lipoprotein Levels in Normal and
Hyperlipidemic Mice, a Proposed Model for Drug Screening. Olivier,. . .

DETDESC:

DETD(415)

TABLE 3

HYPOLIPIDEMIC ACTIVITY OF DIPHOSPHONATES OF FORMULA (I) AND REFERENCE DRUGS

Compounds (I)	Cholesterol (% control)	**Triglycerides** (% control)
1	-2	-28
2	+6	-17
4	-12	-1
. . .		
43	-5	-14
46	+1	-12
47	-31	-45
48	-21	-36
Reference Drugs		
Clofibrate	+4	-5
Gemfibrozil	-7	-35
Fenofibrate	-15	-2

US PAT NO: 4,175,130 [IMAGE AVAILABLE] L1: 10 of 12

SUMMARY:

BSUM(51)

Table 1

Compound	Dose (mg/kg/day)	Decrease (%) Cholesterol	Decrease (%) **Triglyceride**	Increase (%) Liver Weight
A	100	40*	33*	5
B	100	37*	33*	-6
C	100	40*	29*	15
D	100	32*	33*	5
Clo-**fibrate**	100	32*	34*	17*

(*:p<0.05)

US PAT NO: 4,053,635 [IMAGE AVAILABLE] L1: 11 of 12

SUMMARY:

BSUM(9)

TABLE III

Treatment	Cholesterolemia **Triglyceridemia**.degree. mg/100 ml .+-. SE mg/100 ml .+-. ES	Hepatic Cholesterol.degree. mg/g fresh tissue mg/g fresh tissue. . . I	Hepatic **triglycerides**
hyperlipemia from diet* (6)	142.4.+-.7.7(not signif) 91.5.+-.13.6(not si gnificat.)	20.2.+-.0.9(not signific.) (p<0.02)	37.7.+-.5.6
idem + chlo-**fibrate** (9)	138.8.+-.10.7 (" ") 60.0.+-.4.3 (p<0.01)	18.5.+-.1 (" ")	30.3.+-.2.5(p<0.001)
idem + IIIb (7). . .			

SUMMARY:

BSUM(12)

TABLE IV

hypertriglyceridemia from ethanol*

Treatment	Triglyceridemia mg/100 ml .+-. SE	Significance against controls	Significance against sets treated with ethanol
controls (10)	74.20.+-.3.70.	.	.
idem + I (9)	275.11.+-.31.63	--	p<0.001
idem + chlo-fibrate (10)	121.50.+-.12.26	--	not significant
idem + IIId (9)	90.0.+-.14.83	--	p<0.05

*Animal: Sprague-Dawley male rat of the average weight of 150.

US PAT NO: 4,008,324 [IMAGE AVAILABLE] L1: 12 of 12

SUMMARY:

BSUM(31)

Table 1

	Normal diet		Hypercholesterol diet	
	Reduc-tion of Triglycerides	Reduc-tion of Cholesterol	Reduc-tion of Triglycerides	Reduc-tion of Cholesterol

Compound	mg/kg									
	mg/%	%	mg %	%	mg %	%	mg %	%		
Control										
	--.	.	.	65.8*	-24.4					
						288.6	-9.5			
								70.9*	--17.6	
Control										
	--	76.9	--	123.8	--	358.6	--	86.4	--	
Clo-fibrate										
	250	56.1*								
			27.0							
				66.5*						
					46.3					
						347.9	3.0			
								75.6	12.5	
Control										
	--	95.7	--.	.	.					

Triglycerides
tion

```
Trying 01180...Open

PLEASE ENTER HOST PORT ID:
PLEASE ENTER HOST PORT ID:x
LOGINID:d153gsk
PASSWORD:
TERMINAL (ENTER 1, 2, 3, 4, OR ?):□3

* * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
*                                                                     *
*           Welcome to MESSENGER (APS Text) at USPTO                  *
*                                                                     *
*                                                                     *
*    The USPTO production files are current through:                  *
*    APRIL 06,1999  for U.S. Patent Text Data.                  *
*    APRIL 06,1999  for U.S. Current Classification Data.       *
*    APRIL 06,1999  for U.S. Patent Image Data.                 *
*                                                                     *
* * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
   AFTER PRODUCTION HOURS (AT 10:00 P.M.) ON WEDNESDAY, 01/27/99,
   SEVERAL PTONET DEVICES WILL BE RECONFIGURED TO ENHANCE
   NETWORK OPERATIONS.  USERS OF PATENT EXAMINER SEARCH TOOLS
   MUST RE-BOOT THEIR INDIVIDUAL DESKTOP WORKSTATIONS AT THE
   START OF THE BUSINESS DAY ON THURSDAY, 01/28/99 TO INSURE
   THAT NECESSARY FILES ON THEIR WORKSTATION GET UPDATED.  THIS
   WILL ENSURE IMMEDIATE AND ACCURATE ACCESS TO ALL OF THE
   PATENT EXAMINER SEARCH TOOLS.  THANK YOU FOR YOUR COOPERATION
* * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
*       * PLEASE USE 305-9000 FOR NEW TELEPHONE NUMBER *             *
*                                                                     *
* * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
* More U.S. patent data is now available on APS.  The new            *
* USOCR file contains patents issued in 1970, plus some              *
* patents that were missing from the USPAT file.  See the            *
* Patents News Folder under the Public Folders in e-mail for         *
* more information on using the new file.  Thank you.                *
* * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
*  DISCLAIMER:                                                        *
*  Neither the United States Government, nor any agency              *
*  thereof, nor any of their contractors, subcontractors or          *
*  employees make any warranty, expressed or implied,                *
*  including any warranty of marketability of fitness for a          *
*  particular purpose; nor assumes any legal liability or            *
*  responsibility for any party's use, or the results of             *
*  such, of the data.                                                *
* * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
*                Help Desk --> 703-305-9000                           *
*                                                                     *
*    The Help Desk is staffed for APS support 7 days/week.            *
```